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EPIDEMIOLOGY, RISK FACTORS AND DIAGNOSTIC METHODS OF OSTEOPOROSIS. LITERATURE REVIEW

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Abstract

Relevance: The problem of osteoporosis is increasing due to the increase in the population average life expectancy. The incidence of osteoporosis and other degenerative musculoskeletal diseases is expected to continue to increase. The high prevalence of osteoporosis, especially in the presence of fractures, entails high medical and non-medical economic costs in the management of these patients, which determines the importance of this problem for the world health care.

Objective: To review current and relevant studies on the epidemiology, risk factors and diagnosis of osteoporosis.

Search Strategy: This review article analyzes the literature on the epidemiology of osteoporosis, risk factors for its development, and diagnostic methods used to detect this disease. A search was conducted using scientific databases and specialized search engines such as PubMed, Google Scholar, Cochrane Library, Scopus and Web of Science for the last 13 years. *The inclusion criteria* were original articles, systematic reviews and meta-analyses in English and Russian. As a result, 67 literature sources were selected for critical appraisal.

Results and Conclusions: Analysis of available literature data showed different prevalence of osteoporosis depending on geographical location: Iran - 49%, Italy - 18.7%, China - 13%, USA-11%.

Osteoporosis risk factors can be either modifiable or non-modifiable. The most common osteoporosis risk factors have been found to be decreased vitamin D, reproductive disorders, as well as endocrine pathology, gastrointestinal diseases, and other osteoporosis-associated conditions.

Among risk factors, there is little data on the influence of radiation on the development and progression of osteoporosis, although for some regions of the world this factor is significant, due to the activities of nuclear test sites, the consequences of man-made disasters with radiation leakage into the environment.

Dual-energy X-ray absorptiometry (DXA) remains the gold standard in the diagnosis of osteoporosis and is also preferred for determining the efficacy of osteoporosis therapy.

Keywords: *diagnosis, osteoporosis, prevalence, risk factors.*

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Резюме

ЭПИДЕМИОЛОГИЯ, ФАКТОРЫ РИСКА И МЕТОДЫ ДИАГНОСТИКИ ОСТЕОПОРОЗА. ОБЗОР ЛИТЕРАТУРЫ.

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Актуальность: Проблема остеопороза возрастает в связи с увеличением средней продолжительности жизни населения. Ожидается, что заболеваемость остеопорозом и другими дегенеративными заболеваниями опорно-

двигательного аппарата будет продолжать расти. Высокая распространенность остеопороза, особенно при наличии его прямых осложнений - переломов, влечет за собой высокие медицинские и немедицинские экономические затраты при введении этих пациентов, что определяет важность данной проблемы для здравоохранения стран мира.

Цель: Провести обзор современных и актуальных исследований по эпидемиологии, факторам риска и диагностике остеопороза.

Стратегия поиска: В данной обзорной статье проведен анализ литературы, посвященной эпидемиологии остеопороза, факторам риска его развития, а также диагностическим методам, используемым для выявления этого заболевания. Был проведён поиск публикаций в научных базах данных и специализированных поисковых систем, таких как PubMed, Google Scholar, Cochrane Library, Scopus и Web of Science за последние 13 лет. *Критериями включения* стали оригинальные статьи, систематические обзоры и мета-анализы на английском и русском языках. В итоге для критической оценки было отобрано 67 источников литературы.

Результаты и выводы: Анализ доступных литературных данных показал различие по распространенности остеопороза в зависимости от географического расположения: Иран - 49%, Италия – 18.7%, Китай – 13%, США-11%.

Факторы риска остеопороза могут быть как модифицируемые, так и немодифицируемые. Наиболее распространенными факторами риска остеопороза оказались снижение витамина D, нарушения репродуктивной функции, а также эндокринная патология, заболевания желудочно-кишечного тракта и другие, ассоциированные с остеопорозом состояния.

Среди факторов риска мало данных по влиянию радиации на развитие и прогрессирование остеопороза, хотя для отдельных регионов мира данный фактор является существенным, в виду деятельности ядерных испытательных полигонов, последствий техногенных катастроф с утечкой радиации в окружающую среду.

В диагностике остеопороза золотым стандартом остается метод двухэнергетическая рентгеновская абсорбциометрия (DXA-от англ. Dual-energy X-ray Absorptiometry).

Ключевые слова: *диагностика, остеопороз, распространенность, факторы риска.*

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Түйіндеме

ОСТЕОПОРОЗДЫҢ ЭПИДЕМИОЛОГИЯСЫ, ҚАУІП ФАКТОРЛАРЫ ЖӘНЕ ДИАГНОСТИКАЛЫҚ ӘДІСТЕРІ. ӘДЕБИЕТТІК ШОЛУ.

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Өзектілігі: Остеопороз проблемасы халықтың орташа өмір сүру ұзақтығының артуына байланысты артып келеді. Остеопороз және тірек-қимыл аппаратының басқа дегенеративті ауруларының жилігі өсе береді деп күтілуде. Остеопороздың жоғары таралуы, әсіресе оның тікелей асқынулары - сынықтар болған кезде, осы пациенттерді енгізу кезінде жоғары медициналық және медициналық емес экономикалық шығындарға әкеледі, бұл осы проблеманың әлем елдерінің денсаулығы үшін маңыздылығын анықтайды.

Мақсаты: Остеопороздың эпидемиологиясы, қауіп факторлары және диагностикасы бойынша заманауи және өзекті зерттеулерге шолу жасау.

Іздеу стратегиясы: Бұл шолу мақаласында остеопороздың эпидемиологиясына, оның даму қаупінің факторларына, сондай-ақ осы ауруды анықтау үшін қолданылатын диагностикалық әдістерге арналған әдебиеттерге талдау жасалды. Соңғы 13 жыл ішінде PubMed, Google Scholar, Cochrane Library, Scopus және Web of Science сияқты ғылыми мәліметтер базасы мен арнайы іздеу жүйелерін қолдана отырып, жалпыға қол жетімді басылымдарды іздеу жүргізілді. Ағылшын және орыс тілдеріндегі түпнұсқа мақалалар, жүйелі шолулар және мета-талдаулар қосу критерийлері болды. Нәтижесінде сыни бағалау үшін 67 әдебиет көзі таңдалды.

Нәтижелер мен қорытындылар: Қолда бар әдеби деректерді талдау географиялық орналасуына байланысты остеопороздың таралуы бойынша әр түрлі көрсетті: Иран - 49%, Италия – 18.7%, Қытай – 13%, АҚШ-11%.

Остеопороз қауіп факторлары өзгермелі болуы мүмкін, мұнда араласу аурудың ағымын өзгерте алады және өзгертілмейтін, оларды өзгерту немесе жою мүмкін емес. Д витаминінің төмендеуі, репродуктивті функцияның

бұзылуы, сондай-ақ эндокриндік патология, асқазан-ішек жолдарының аурулары және остеопорозбен байланысты басқа жағдайлар остеопороз үшін ең көп таралған қауіп факторлары болды.

Тәуекел факторларының арасында радиацияның остеопороздың дамуы мен прогрессиясына әсері туралы деректер аз, дегенмен әлемнің жекелеген өңірлері үшін бұл фактор ядролық сынақ полигондарының қызметіне, радиацияның қоршаған ортаға ағып кетуімен техногендік апаттардың салдарына байланысты маңызды болып табылады.

Остеопорозды диагностикалауда Қос энергиялы рентгендік абсорбциометрия әдісі Алтын стандарт болып қала береді (DXA-ағылш. Dual-energy X-ray absorptiometry), ол остеопороз терапиясының тиімділігін анықтау үшін де қолайлы.

Түйінді сөздер: *диагностика, остеопороз, таралуы, қауіп факторлары.*

Дәйексөз үшін: *Касымова М.Н., Иванова Р.Л., Горемыкина М.В., Тукинова А.Р., Ногаева М.Г.* Балалар мен жасөспірімдердегі сүйек алмасуындағы биохимиялық маркерлардың рөлі. Әдебиеттік шолу // Ғылым және Денсаулық сақтау. 2025. Vol.27 (2), Б. 207-218. *doi 10.34689/SH.2024.27.2.023*

Introduction

The relevance of the problem of osteoporosis (OP) is increasing due to the increase in the average life expectancy of people, which lasts for more than 30 years. Aging and OP are closely related: the risk of developing OP and fractures increases with aging [18]. Demographic aging of the population has a significant impact on human health, as well as on the structure of incidence and mortality. The share of degenerative diseases of the musculoskeletal system, among which OP occupies an important place, is expected to grow significantly [41]. Studies show that one in three women over the age of 50 suffers from OP, and more than 33% of women over the age of 65 have vertebral body fractures. In addition, more than 36% of patients with femoral neck fracture die within the first year after injury, and more than 50% of survivors become disabled [24].

OP is one of the most common chronic disease in the world. Hundreds of millions of people are affected each year, and many more are at risk. The main sign of OP is fractures due to bone fragility, which severely impairs the quality and length of life and places a serious financial burden on society [28]. A number of authors describe OP as a condition characterized by a decrease in bone density and strength, which increases the risk of fracture with minor trauma [32, 45].

The relevance of OP is due to the prevalence of the disease, which requires attention and a comprehensive approach to prevention and treatment. Approximately 10% of the world's population and 30% of postmenopausal women suffer from this disease. Fractures are a serious complication of OP and a major cause of morbidity and mortality in the elderly population [23]. Although the structure of the fracture does not always determine the degree of OP, the fracture may arise from additional factors-the mechanism of injury.

The purpose of this article is to systematize and analyze the existing literature on the epidemiology of OP, risk factors for its development, and diagnostic methods used to detect this disease.

Search Strategy: During the study, we searched for open access publications, using scientific databases and specialized search engines such as PubMed, Google Scholar, Cochrane Library, Scopus and Web of Science. We analyzed a number of original articles and review papers on the topic published in the last 13 years. The keywords used in the search were: diagnosis, OP, prevalence, and risk factors. The inclusion criteria were original articles, systematic reviews and meta-analyses in English and Russian. At the same time, expert opinions in the form of short communications, repetitive publications, and articles with unclear conclusions were excluded from the analysis. As a result, 67 literature sources were selected for critical appraisal.

Results

Epidemiology

Coding of OP in medical records is performed according to the International Classification of Diseases X revision (M80.0) According to a systematic review, OP causes significant economic losses to the health care system, with annual costs ranging from 5 to 10 billion dollars in the United States alone. Various fractures, especially of the spine, result in decreased quality of life, long-term hospitalization, disability, and increased mortality. The prevalence of OP in the elderly population varies from country to country, ranging from 7.9% in Iran to 49% in Nepal. It is estimated that approximately one in three women and one in five men over 50 years of age experience osteoporotic fractures. Statistically, one in five patients with pelvic fracture dies within a year [57]. A 2013-2014 U.S. study reported that 6 to 11% of adults aged 50 years and older, representing 1 in 9 to 1 in 17 adults, had OP. The prevalence of OP was higher among non-Hispanic Asians compared to other racial/ethnic groups analyzed using data on young white women [46]. In the European Union, OP is a serious problem affecting a significant number of women and men. The disease often goes undetected until fractures occur, which has led to its name as a “silent epidemic”. Despite advances in risk assessment and treatment, OP remains underdiagnosed and undertreated. In Italy, the prevalence of OP is approximately 18.7% and of osteopenia approximately 42.6% [30]. According to the study, about 13% of the population in China suffers from OP, and the number of fractures due to this condition may increase to 4.83 million per year by 2035. Currently, about 10.9 million men and 49.3 million women aged 50 years and older in China suffer from OP. A study by *Q. Zeng et al.* (2019) showed that the prevalence of OP is 6.46% among men and 29.13% among women in the age group of 50 years and older [65]. Globally, osteopenia and OP have become more prevalent than ever before with 40.40% and 19.75%, respectively. The burden of these diseases has increased significantly between 1990 and 2019s, with disability life years and mortality rates increasing by 93.82% and 111.16%, respectively. The situation is particularly alarming in China, which is among the five countries with the highest DALYs from osteopenia-related fractures and OP, with an increase of 121.07% and 148.65%, respectively, over this period [35]. In a study *by M. Zheng et al.* (2023) compared the prevalence of OP and found that males

had lower prevalence of OP (2.68%) compared to females (13.82%) [66]. The authors studied the prevalence of OP in the Asia-Pacific region and found that OP-related fractures varied greatly by region. Also, the incidence rate increased with age and ranged from 10 to 30% among women over 40 years of age and up to 10% among men in seven developed countries in the region. The incidence of osteoporotic fractures ranged from 500 to 1,000 cases per 100,000 person-years among adults over 50 years of age. Both rates generally increased with age and were higher in women. The authors make recommendations that governments and health systems should consider effective methods of preventing, diagnosing, and treating OP in order to reduce health care costs and fracture-related mortality [31].

In developing countries, with the increasing number of elderly and the adoption of Western lifestyles, the burden of OP is increasing. Over the past 25 years, many risk factors for bone loss have been identified and effective treatments for OP have been developed, but only a small proportion of patients receive the necessary treatment [33].

According to *Lesnyak O.M. and co-authors,* in Russia, OP is diagnosed in every third woman and every fourth man aged 50 years and older. Every minute there are 7 vertebral fractures in the country, and every 5 minutes there is a fracture of the proximal femur. The total number of major osteoporotic fractures is projected to increase from 590,000 to 730,000 cases per year by 2035. Epidemiologic studies have found that OP therapy is required for 31% of women and 4% of men over 50 years of age due to high fracture risk [12].

The prevalence of primary OP as an independent disease without identifying another cause of reduced skeletal strength, occupies 95% in the structure of OP in postmenopausal women (postmenopausal OP) and 80% in the structure of OP in men over 50 years of age [6, 14, 26].

The continuing trend of population aging allows us to predict an increase in the number of osteoporotic fractures worldwide. An international team of authors studying the problems of epidemiology in Uzbekistan, Kazakhstan and the Kyrgyz Republic noted that the number of osteoporotic fractures in these countries is likely to increase by 2.5 - 3.5 times by 2050 [8].

The population of Kazakhstan is projected to increase by 13.4% by 2035 and by 24.8% by 2050. The number of people over 50 years of age is expected to increase by 35% and over 70 years of age by 95%. By 2050, the number of elderly people over 50 is expected to increase by 64% and over 70 by 15.2%. Examination of the indicators of official statistics in Kazakhstan for 2012 and 2016 showed that there was an increase in the overall incidence of OP by 39.5%, and the number of new diagnoses increased by 23.7%. Projections for 2050 show a significant increase in hip fracture cases by 140%, especially among women (153%), while in men the increase will be 112%. The probability of a proximal femur fracture for people over 50 is 7.7% for women and 4.3% for men. The number of patients with distal forearm and proximal humerus fractures is also expected to nearly double by 2050 [4].

A study conducted in the city of Semey revealed a high frequency of osteopenic syndrome (68%) among adolescents and young adults living in areas adjacent to the Semipalatinsk nuclear test site. Decrease in bone mineral density is more frequently observed in young men (76%) compared to girls (64%). In 88% of adolescents, osteopenia was combined with hypocalcemia and hypophosphoremia. The study emphasizes the need to further study the risk factors of OP among young people living in environmentally unfavorable conditions, with the creation of a control group [9].

Thus, worldwide, OP is widespread and tends to further progression, which is confirmed by the data of the above authors.

Risk factors for developing osteoporosis

Osteoporosis represents one of the fastest growing health problems in the world, with many factors influencing its development [42].

As is known, all risk factors (FRs) of OP development are divided into two groups: modifiable, i.e., those in which active intervention can change the course of the disease and non-modifiable, change or elimination of which is not possible [13, 34].

Modifiable factors include smoking, low body weight, calcium and vitamin D deficiencies, excessive alcohol and caffeine consumption, frequent falls, lack of physical activity, and taking certain medications [2].

Osteoporosis in postmenopausal women may be associated with low body mass index (BMI), calcium and vitamin D deficiency, prolonged kyphosis, and lack of outdoor physical activity [59].

In the article by D. V. Akimova (2014) the main FRs of osteoporosis development are given, such as genetic features, gender, age, nutrition, activity level, as well as the influence of alcohol consumption and smoking. The influence of industrial factors such as exposure to fluoride, aluminum, cadmium, phosphorus, as well as local and general vibration on the development of OP is also considered [1].

In the study by *G. A. Saneeva et al.* (2015) studied the structure and prevalence of the main FRs of OP and fractures in 86 postmenopausal and senile women with OP. The diagnosis of OP was confirmed by the presence of a low-energy fracture and/or the corresponding osteodensitometric T-criterion. The authors conducted a survey to identify OP and fracture FRs according to clinical guidelines using the Fracture Risk Assessment Tool (FRAX). The most common FRs were vitamin D deficiency, prior fractures, reproductive disorders, and various somatogenic causes of secondary OP, including endocrinopathies, gastrointestinal diseases, and other OP-associated conditions including cardiovascular disease [15].

Verbova A. F. et al. (2017), studying non-modifiable factors, highlighted age (over 65 years), female gender, previous fractures, presence of fractures in close relatives, long-term use of glucocorticosteroids, white race, periods of immobilization, dementia and hormonal factors. It has been observed that age plays an important role in bone mass because there is a natural decrease in bone density and strength with age. In women, bone mass loss is about 0.86-1.21% annually, while in men it reaches 0.04-0.90% [2].

According to the literature, both external conditions and genetic inheritance can serve as FRs of OP development [22]. These factors, alone or in combination, can significantly reduce bone density and cause OP to develop [48]. Recent studies suggest that unfavorable lifestyle

factors play an important role in accelerated bone mineral density loss in postmenopausal women [67].

A study of the FRs of OP development in men over 50 years of age has shown that many of them, usually associated with postmenopausal women, also affect men. The major FRs of bone loss in men include: previous fractures after age 40, glucocorticoid use for more than 3 months, age older than 65 years, heredity, alcohol abuse, calcium and vitamin D deficiency, testosterone deficiency, low body weight, smoking, and use of hormonal medications. Patients with multiple FRs have a significantly increased likelihood of fracture. In men, secondary OP is relatively common (30-60%) [5, 55, 62].

In a study conducted in Pakistan, it was found that apart from age, a number of factors such as bone fractures, family history, physical activity, family size, meat consumption, type of delivery, breastfeeding, premature menopause, loss of appetite and use of anticoagulants have statistically significant association with increased risk of developing OP [64]. In a study by *M. Zheng et al.* (2023) found that among women, the risk of OP was significantly higher in postmenopausal (30.34%) compared to premenopausal (4.78%). In addition, that OP was more common in rural population (10.33%) compared to urban population (5.52%). In urban FR osteoporosis in men included older age, hypertension, marital status (divorced, widowed and unmarried), smoking, family history of OP, dyslipidemia and elevated β-CTX levels. On the other hand, higher level of education and a diet including rice/ pasta and water products were associated with a reduced risk of OP in men. Similar results were also obtained in rural areas [66]. A study in Urmia city in Iran showed that the prevalence of OP was 42.2%, with a prevalence of 14.3% in women under 45 years of age and 50.7% in women over 45 years of age. Education level, history of fracture, presence of chronic diseases, number of pregnancies and deliveries, duration of breastfeeding, nutrition and green tea consumption had a significant association with bone mineral density (BMD). Regression analysis showed that age, fracture history and pregnancy were significant FRs of osteoporosis, while BMI was a protective factor [56]. In a study by *C. Neglia et al.* (2016) found that individuals with diabetes and obesity had a significantly higher risk of developing OP, with odds ratios (OR) of 1.39 (CI: 1.05-1.83) and 1.46 (CI: 1.20-1.78), respectively. There was also a statistically significant trend of increasing risk of OP with increasing BMI. These results confirm the significant influence of obesity, type 1 and type 2 diabetes on OP development [50]. Korean researchers conducted a study in which they investigated the relationship between gout and OP. Their results showed that patients with gout had an increased risk of developing OP in all age groups except those over 80 years of age. Gout was found to be a FR for osteoporosis with a risk ratio of 1.48 (95% CI: 1.45-1.51, $p < 0.001$). Women had an increased risk of OP with its peak at age 70 years. Of particular interest, men in their 20s with gout had almost four times the risk of developing OP than patients without gout [44]. A study by Azuma K. et al. (2015) showed that prolonged psychological stress increases the likelihood of developing OP through various interaction pathways in the body. This is due to the important function of the hypothalamus in the regulation of bone metabolism. The effects of stress on the body include decreased bone density and impaired bone quality, affecting various systems such as the hypothalamic-pituitary-adrenal axis and the sympathetic nervous system. Interestingly, active chewing, as a stress-responsive response, can reduce the negative effects of stress on the body, including bone mass loss. Thus, active chewing may be a useful method in the prevention and treatment of OP caused by chronic stress [21].

The main risk factors for the development of OP are summarized in Table 1.

Radiation, as one of the unmodifiable FRs of osteoporosis, remains an insufficiently studied problem, although it may contribute significantly to its development. Anatomical and physiological changes in bone tissue under the influence of ionizing radiation may be associated with impaired osteoblast and osteoclast activity, the key cells responsible for bone formation and resorption. These changes may lead to decreased bone strength and increased bone fragility. Although data on the effects of radiation on OP are still limited, some studies already suggest a link between radiation exposure and bone deterioration. This emphasizes the need for more research in this area.

L.E. Sivordova et al. (2014) conducted a study of the main epidemiological and pathogenetic characteristics of OP in persons exposed to radiation during the liquidation of the consequences of the Chernobyl nuclear power plant accident. The results of the study showed that liquidators of the accident had a high incidence of OP, which was accompanied by bone and spine pain, decreased muscle strength, history of fractures, and symptoms of hypocalcemia, such as cramps in calf muscles. Analysis of markers of bone metabolism revealed decreased osteoblast activity with normal osteoclast function. Thus, in radiation-exposed individuals, there was an imbalance in bone metabolism, expressed as a decrease in bone formation with preservation of normal bone resorption [16]. In a study conducted in Kazakhstan by Gabdulina G.H. et al. the level of OP detection using ultrasound screening diagnostics in the East Kazakhstan region was 11.8%, while the all-republican level reached 19.4%. A significant part of the examined patients had osteopenia, which was detected in 69.4% of them [3]. In the studies by *G.A. Tanysheva et al.* (2014), conducted in the areas exposed to radiation as a result of nuclear tests at the Semipalatinsk test site, the frequency and degree of decrease in bone mineral density in women of reproductive age were determined. Statistically significant correlations between the level of irradiation of ancestors of II and III generations and MDB indices in their descendants, women of reproductive age, were revealed. The results allow us to assert a more rapid development of involutional OP in female descendants exposed in the II and III generations [19].

However, these studies were performed only with the help of ultrasound screening test, which refers to the screening diagnosis of persons with suspected OP and is not a method of accurate diagnosis of OP, so the results of these authors, in our opinion, are inconclusive. For accurate diagnosis of OP, there are other, more informative methods such as DXA today.

Exposure from radiation can be detrimental to health, with adverse effects of radiation exposure occurring after a latent period throughout life [16]. In this regard, scientific and practical research aimed at studying the remote radiation effects become relevant.

Table 1.

Major risk factors for osteoporosis and bone fractures.

Modifiable risk factors	Non-modifiable risk factors
Tobacco smoking	Age over 65
Insufficient calcium intake	Female gender
Vitamin D deficiency	White (Caucasian) race
Alcohol abuse	Previous fractures
Low physical activity	Low bone mineral density
Tendency to fall	Heredity (family history of osteoporosis)
BMI<20 kg/m2 and/or weight less than 57 kg	Hypogonadism in men and women
	Decrease in creatinine clearance and/or glomerular filtration rate
	Systemic GC intake for more than three months
	Long-term immobilization
Vitamin A excess	Genetic diseases (porphyria, cystic fibrosis, Ehlers-Danlo syndrome, Gaucher disease, glycogen storage diseases, Marfan syndrome, “steel hair” disease (Menkes disease) - copper transport disorder, osteogenesis imperfecta, etc.).
Excess salt in the diet	Endocrine disorders (acromegaly, endogenous hypercorticism, type 1 and type 2 diabetes mellitus, thyrotoxicosis, hyperparathyroidism)
Medications (aluminum (in antacids), anticoagulants, anticonvulsants, anticancer drugs, premenopausal contraception, methotrexate)	Gastrointestinal disorders (celiac disease, gastric bypass, gastrointestinal surgery, inflammatory bowel disease (Crohn's disease and nonspecific ulcerative colitis), malabsorption, etc.).
Parenteral nutrition	Hematologic disorders (hemophilia, leukemia and lymphomas, monoclonal gammopathies, multiple myeloma, thalassemia, sickle cell anemia, systemic mastocytosis)
	Rheumatologic and autoimmune diseases (ankylosing spondylitis, rheumatoid arthritis, systemic lupus erythematosus)
	Neurological and musculoskeletal risk factors (epilepsy, muscular dystrophy, spinal cord injury)
	Other conditions and diseases (terminal renal failure, sarcoidosis, post-transplant bone disease)

Methods of diagnosing OP

Currently, several methods are used to diagnose OP: laboratory with the determination of bone metabolism products to determine the function of osteoblasts and osteoclasts; instrumental with the use of various methods of radial diagnosis; method of using FRAX counting with the calculation of the possibility of fractures with the test; bone biopsy; method of determining gene markers.

Laboratory diagnostics is an important part of the evaluation of patients with OP. General blood and urine tests help to identify possible signs of secondary OP; they complement the data obtained by other methods of bone tissue examination, expanding the possibilities of OP diagnosis [38].

For example, clinical blood tests can detect anemia, inflammatory processes and other general health conditions. Biochemical blood tests: determination of calcium, magnesium and phosphorus levels helps to assess bone metabolism; PTH may be elevated in OP, indicating abnormalities in calcium metabolism; vitamin D deficiency may lead to decreased calcium absorption and bone deterioration; elevated alkaline phosphatase levels may indicate bone pathology. Analysis for levels of specific markers of bone resorption, such as deoxypyridinoline (DPD) or collagen N-telopeptide (NTx), can help assess the rate of bone resorption. Markers of bone formation, such as osteocalcin or procollagen I N-telopeptide (PINP), can provide insight into the rate of bone formation. In addition, levels of sex hormones (estrogen and testosterone) may be examined, as their deficiency may contribute to the development of OP. Tests for diseases that affect metabolism, such as tests for thyroid disease, diabetes mellitus, and other endocrine disorders, are also used [36].

Bone metabolic markers are used to measure peptides produced during bone matrix formation or degradation. Among them are indicators of bone formation that reflect the activity of osteoblasts, the cells responsible for bone formation. Examples of such markers are alkaline phosphatase (ALP) and osteocalcin (OC). Alkaline phosphatase is secreted by various tissues, but the bulk is found in liver and bone (about 90%) [47]. The bone isoform is the same in both sexes and is independent of circadian rhythm, making it a simple marker for metabolic bone disorders despite its low sensitivity and specificity. With increased bone turnover, the half-life of OC decreases, leading to its excretion with urine [29].

Currently, the use of biomarkers of bone metabolism is a convenient and effective method for additional diagnosis and assessment of the effectiveness of osteoporosis therapy. Biomarkers, such as N- and C-telopeptides of

collagen, as well as alkaline phosphate, are able to reflect the changes occurring in bones. Unlike MDB measurements, which take time to detect changes, biomarkers provide results much more quickly. It is recommended to analyze the level of biomarkers 3 months after the start of therapy, and an increase in their content by 30% or more may indicate the effectiveness of treatment. However, it should be taken into account that the use of biomarkers for the diagnosis of OP should be accompanied by densitometry [7].

Strukov V. et al. in their study investigated the possibility of OP diagnosis, including both biochemical markers of bone metabolism, such as osteocalcin, parathormone, 25(OH)D and β-CrossLaps in serum, and instrumental diagnostic methods. They noted that although histologic analysis of iliac crest biopsy is considered the most reliable method for the diagnosis of OP, its use is limited due to its invasiveness. Radiography is more readily available but may fail to detect OP when bone mass loss is less than 30-40%. X-ray absorptiometry is the most accurate method for assessing MDB and determining the degree of OP based on it [17].

Bone resorption markers such as pyridinolines (Pir), deoxypyridinoline (Dpir), as well as ICTP, β-CTX and NTX peptides are widely used in clinical practice. The markers β-CTX and NTX are commonly used for the diagnosis of OP. There are other methods to assess bone density such as ultrasound and quantitative computed tomography, but the most common method is DEXA. A bone biopsy is only ordered when a tumor is suspected [37].

The Bone Health and Osteoporosis Foundation (BHOF) recommends a comprehensive diagnosis of OP that includes an assessment of individual fracture risk, patient history, physical examination, and special studies to rule out possible secondary causes of bone fragility. Patients with signs of OP, such as height loss, back pain, or fractures, are recommended to be screened for spinal fractures. Increased fracture risk is most often associated with age, so screening of all older adults is considered essential. Individuals with a history of fracture or high fracture risk should have a more thorough bone health assessment and possibly be referred to a bone metabolism specialist for further monitoring and treatment [27].

According to the World Health Organization (WHO) standards for densitometry, MDB levels are classified as follows: normal - bone mineral density level is above 1 standard deviation from the mean; osteopenia - bone mineral density level is between 1 and 2.5 standard deviations from the mean; OP - bone mineral density level is below 2.5 standard deviations from the mean; established OP - bone mineral density level is below 2.5 standard deviations from the mean and on the [43].

Densitometry helps to assess the risk of fracture, which depends on the degree of OP. A normal value corresponds to a low risk of fracture, an osteopenia value doubles the risk, and an OP value quadruples the risk. Established OP increases the risk by 1.5-2 times for each reduced standard deviation, and severe OP represents a similar risk of established OP [20].

The clinical feature of OP, low-energy fractures, occur most commonly in the spine, hips, and forearms because of their vulnerability. The risk of these fractures increases with age, making them a major cause of morbidity and mortality in the elderly. The most susceptible bone sites for osteoporotic fractures are the upper and lower ends of the hip and shoulder, as well as the spine [51]. Transverse femoral fracture is a severe complication that often results in a high risk of morbidity and mortality [54].

A study conducted in Spain by the International Osteoporosis Foundation used additional diagnostic tests to monitor the effectiveness of osteoporosis treatment [25], including double X-ray absorptiometry (DEXA), which is the most recommended and accurate method for diagnosing osteoporosis. DEXA makes it possible to assess the probability of fractures, prescribe the necessary treatment and monitor its effectiveness 58]. DEXA is a method that quantitatively measures bone mineral density in the axial skeleton, such as the spine and hips. This method is based on measuring the transmission of x-ray photons with two energy peaks through the patient's body to determine the calcium content of the bones [52].

DEXA allows accurate diagnosis of osteoporosis and is a valuable tool for early detection of this disease [61]. Osteoporosis is known to develop when bone mineral density levels fall by more than 2.5 standard deviations from the normal range for healthy young women. Decreases in bone mineral density at different areas of the body are associated with an increased risk of fracture. DEXA scanning, although an effective diagnostic method, is expensive and requires specialized equipment. Therefore, most countries prefer to screen for osteoporosis only for women over 65 years of age, while an opportunistic screening approach is possible for younger women [49], which uses a specialized clinical tool to identify individuals at high risk of OPs [53].

Densitometry is widely used to quantify bone mass. Although osteoporosis is a more complex condition than just a decrease in bone density, measuring bone density plays an important role in diagnosing and predicting fracture risk. This method helps to determine the rate of bone mass loss and monitor the progression of the disease [39].

Klimova J.A. et al. note that for the initial stage of osteoporosis diagnosis it is necessary to identify risk factors based on patient data obtained by questionnaire, such as lack of calcium in the diet, vitamin D deficiency, GI diseases, early menopause, long periods of immobility, taking medications, diseases of various systems, low body weight, bad habits and low physical activity. Radiologic methods are widely used to study bone health, but conclusions about the presence of osteoporosis in the early stages can be made only if there is a significant loss of bone mass (more than 30%). For earlier diagnosis of osteoporosis, bone densitometry is often used to detect a loss of bone mass as early as 2-5%. This method, based on the measurement of bone density, is the standard for diagnosing osteoporosis. Laboratory diagnostic methods are used to assess bone metabolism. Their purpose is to determine the causes of secondary osteoporosis, to exclude other diseases with similar symptoms and to assess the metabolic characteristics of osteoporosis. [10].

Phantom-free computed tomography (CT) calibration methods can significantly improve osteoporosis screening and allow retrospective analysis of imaging data. New advances in hardware are expanding the use of dual-

energy CT and cone-beam CT for bone imaging. Also, improvements in MRI sequences contribute to more accurate assessment of bone properties. The introduction of image registration techniques opens new horizons for the study of soft tissue-bone interactions and bone structure updating. Although DEXA remains the most common method for diagnosing osteoporosis, new imaging technologies are becoming increasingly available and provide important additional information for clinical decisions [60].

Assessment of OP severity and fracture risk

The WHO-developed FRAX tool helps physicians to estimate the likelihood of fractures over the next decade based on a variety of clinical and demographic data. In rheumatology, FRAX can be particularly useful for assessing fracture risk in patients with rheumatoid arthritis and other conditions that can affect bone density. For example, long-term corticosteroid therapy, often used to treat rheumatic diseases, can significantly increase the risk of OP and subsequent fractures. The use of FRAX allows physicians to better plan preventive measures such as lifestyle modification, drug therapy, or other interventions to reduce fracture risk in patients [11]. FRAX models for the Republic of Kazakhstan included the incidence of hip fractures by age and sex and national mortality rates. Probabilities of fractures were compared with similar indicators in neighboring countries with FRAX models. The FRAX 10-year probability model of osteoporotic fractures for the Republic of Kazakhstan was developed by the author Isayeva S. [40].

Among the tools designed to identify women at increased risk of developing OA are the following: SCORE (Simple Calculated Osteoporosis Risk Estimation), ORAI (Osteoporosis Risk Assessment Instrument), OSIRIS (Osteoporosis Index of Risk) and OST (Osteoporosis Self-assessment Tool). Singapore's recommendations also include the use of the OSTA (Osteoporosis Screening Tool for Asian Women), which is specifically designed for this group of women and has been successfully tested in a Japanese sample. The OSTA methodology is based on individualized osteoporosis risk assessment, taking into account age and weight parameters: score = age (years) - weight (kg) [63].

In unclear cases, bone biopsy is used. In recent years, the method of determining gene markers and identifying gene predisposition mechanisms to identify groups of people predisposed to the development of osteoporosis has been used in a fairly targeted manner.

Conclusion

Thus, in the course of our review of the available literature on the epidemiology of osteoporosis, it is clear that this disease is a significant public health problem, affecting millions of people worldwide. Early identification of modifiable and non-modifiable risk factors for the development of osteoporosis allows for timely preventive measures. It should be especially noted that in recent years, the radiation factor has become increasingly important due to technological progress. At the same time, the influence of radiation associated with nuclear testing as one of the non-modifying risk factors of osteoporosis development remains insufficiently studied. The key methods of osteoporosis diagnosis discussed in the literature are densitometry and quantitative ultrasound evaluation of bone tissue, which allows timely detection of the disease and prevention of its progression. However, despite the available modern technologies, detection of osteoporosis at early stages is still a difficult task that requires further research.

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